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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/270,006	03/16/1999	JEAN-PIERRE ROBIN	017753-113	1899

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BURNS DOANE SWECKER & MATHIS L L P
POST OFFICE BOX 1404
ALEXANDRIA, VA 22313-1404

EXAMINER

BALASUBRAMANIAN, VENKATARAMAN

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 05/17/2002

23

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/270,006

Applicant(s)

ROBIN ET AL.

Examiner

Venkataraman Balasubramanian

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 April 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 88-101 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 88-101 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

Continued Prosecution Application

The request filed on 4/29/2002 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/270,006 is acceptable and a CPA has been established. An action on the CPA follows.

Claims 88-101 are pending.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 88-101(previously claims 59-65) are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al. Yaoxue Xuebao (Acta. Pharm. Sinica)27, 178-184, 1992(Wang I) and Huang et al, the Alkaloids, Vol. XXII 157-225, 1984 in view of

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Wang et al. *Yaoxue Xuebao* (Acta. Pharm. Sinica) 27, 173-177, 1992(Wang II) for reasons of record. To repeat:

Wang I teaches the tetrahydrofuran and tetrahydropyran esters of cephalotaxine as noted in the above 102 rejection. See compound 8 and 9. Note these compounds are known to exhibit antitumor activity.

Wang I differs in not making the tetrahydrofuran or pyran carboxylic acid first.

Huang et al. teaches the process for hydrolyzing the cephalotaxine alkaloids and the synthesis of the acid components. See page 165 for mild hydrolysis to get compound 7 and see route 3 on page 166. Wang II teaches a process for cyclizing the open chain acid ie compound 7 bearing a CTX group to the corresponding tetrahydrofuran compound. See page 174 of Wang II and note the last reaction shown at the bottom of the page using TsOH.

Note the starting materials are analogous in that they are compound of formula 7 with a methoxy on the tertiary carboxylic group or CTX. Thus one having ordinary skill in the art at the time of the invention was made would have been motivated to combine both the primary and secondary references and employ the process taught by these prior art to the starting materials and expect to obtain the desired product because he would have expected the analogous starting materials and reactants react similarly. It has been held that application of an old process to an analogous material to obtain a result consistent with the teachings of the art would have been obvious to one having ordinary skill. Note *In re Kerkhoven* 205 USPQ 1069.

Applicants' argument to overcome this rejection as noted in paper 12, is not persuasive.

Applicants argue that instant invention differs in using the chiral acid for making the final product which leads to even with racemate to diastereoisomers or enantiomerically pure product - a benefit not suggested or taught by the cited reference. This is not a valid argument. It is well known in the art that chiral intermediates can be resolved and used for making enantiomerically pure compound or diastereoisomers as the case may be. Hence, one trained in the art would have been motivated to resolve the racemic acid taught by the prior art and use it for synthesis of chiral compounds.

As for applicants' argument (in paper # 15), as noted in the advisory action, following also apply:

1. Contrary to applicants' urging, examiner has made a prime facie case of obviousness. As noted before, Wang I teaches the tetrahydrofuran and tetrahydropyran esters of cephalotaxine. Wang I differs in not making the tetrahydrofuran or pyran carboxylic acid first. Huang et al. teaches the process for hydrolyzing the cephalotaxine alkaloids and the synthesis of the acid components. Wang II teaches a process for cyclizing the open chain acid i.e. compound 7 bearing a CTX group to the corresponding tetrahydrofuran compound. Note the starting materials are analogous in that they are compound of formula 7 with a methoxy on the tertiary carboxylic group or CTX. Thus one having ordinary skill in the art at the time of the invention was made would have been motivated to combine both the primary and secondary references and

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employ the process taught by these prior art to the starting materials and expect to obtain the desired product because he would have expected the analogous starting materials and reactants react similarly.

2. Applicants also argue that it is impossible to arrive at the desired product as Reformatsky reaction will not work in presence of hydroxyl group (see page 3-4 of remarks) but have failed to provide any evidence that such is the case. Contrary to applicants' urging, the Information Disclosure Statement provided by the applicants indicates that the Reformatsky reaction is viable in presence of hydroxyl group(s). See Hudlicky et al. page 663, compound 104.

Hence the rejection is proper and is maintained.

Conclusion

This is a CPA of applicant's earlier Application No. 09/270,006. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application.

Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the

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shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.


Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (703) 305-1674. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM.

The fax phone number for the organization where this application or proceeding is assigned (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

VB
V. Balasubramanian (Bala)

5/14/2002


MUKUND J. SHAH

SUPERVISORY PATENT EXAMINER

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